

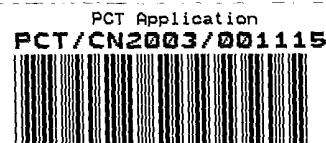
Translation

PATENT COOPERATION TREATY

PCT


INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY  
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)



REC'D 03 APR 2006

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Applicant's or agent's file reference 031211CP		<b>FOR FURTHER ACTION</b> See Form PCT/IPEA/416	
International application No. PCT/CN03/01115		International filing date (day/month/year) 25. Dec. 2003 (25.12.03)	Priority date (day/month/year) 12. Dec. 2003 (12.12.03)
International Patent Classification (IPC) or national classification and IPC See supplemental box			
Applicant Shanghai Institute of Materia Medica, Chinese Academy of Sciences et al			
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>8</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic _____, containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>			
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input checked="" type="checkbox"/> Box No. VIII Certain observations on the international application</p>			
Date of submission of the demand 11. Jul. 2005 (11.07.2005)		Date of completion of this report 06. Mar. 2006 (06.03.2006)	
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## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.  
PCT/CN03/01115

## Box No. I Basis of the report

1. With regard to the **language**, this report is based on:

- ☒ the international application in the language in which it was filed
- ☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of:
- ☐ international search (Rules 12.3(a) and 23.1(b))
- ☐ publication of the international application (Rule 12.4(a))
- ☐ international preliminary examination (Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

- ☒ the international application as originally filed/furnished
- ☐ the description:
- pages \_\_\_\_\_ as originally filed/furnished
- pages \* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- pages \* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☐ the claims:
- pages \_\_\_\_\_ as originally filed/furnished
- pages \* \_\_\_\_\_ as amended (together with any statement) under Article 19
- pages \* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- pages \* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☐ the drawings:
- pages \_\_\_\_\_ as originally filed/furnished
- pages \* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- pages \* \_\_\_\_\_ received by this Authority on \_\_\_\_\_
- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (*specify*): \_\_\_\_\_
- ☐ any table(s) related to sequence listing (*specify*): \_\_\_\_\_

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (*specify*): \_\_\_\_\_
- ☐ any table(s) related to sequence listing (*specify*): \_\_\_\_\_

\* If item 4 applies, some or all of those sheets may be marked "superseded."

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

This questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 9

because:

☒ the said international application, or the said claims Nos. 9

relate to the following subject matter which does not require an international preliminary examination (*specify*):

The invention set forth in Claim 9 relates to a method for treatment of the human body by therapy.

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_ are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. \_\_\_\_\_

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13ter.1(a) or (b) and 13ter.2.

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.  
PCT/CN03/01115**Box No. V** Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement

## 1. Statement:

Novelty (N)

Claims 1-4 (part), 5, 6-7 (part), 8 YESClaims 1-4 (part), 6-7 (part) NO

Inventive step (IS)

Claims 1-8 (part) YESClaims 1-8 (part) NO

Industrial applicability (IA)

Claims 1-8 YES

Claims \_\_\_\_\_ NO

## 2. Citations and explanations (Rule 70.7)

See supplemental box

**Box No. VIII** Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1-3 relate to the glucagon-like peptide-1 receptor agonists, wherein the Ar<sub>1</sub> and Ar<sub>2</sub> groups were defined too broad, including an extremely large number of compounds. However, only a very small part of compounds claimed by claims 1-3 were supported by the description, such as the compounds wherein Ar<sub>1</sub> was phenyl substituted by a thiophenylformyloxy group. Therefore, the claims 1-3 lack support, not meeting the criteria mentioned in Article 6 PCT.

## Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box No.V 2.Citations and explanations

2.1 The following documents have been cited herein:

Document 1: JP3-50532A

Document 2: JP9-244229A

Document 3: JP11-273865A

Document 4: Shafi, P. M. et al., "A new synthetic route to 4-arylidene-2-phenyl-2-imidazolin-5-ones", Indian J. Chem., Sect. B:Org. Chem. Incl. Med. Chem., 1999, 38B(3), p378-379

Document 5: Agarwal, Rajesh et al., "Synthesis of 2-aryl-1-(4-morpholinophenyl)-4-(3,4-disubstituted-benzylidene)imidazolin-5-ones as CNS active agents", Indian J. Chem., Sect. B, 1983, 22B(3), p308-310

Document 6: Follenius-Wund, Anny et al., "Fluorescent derivatives of the GFP chromophore give a new insight into the GFP fluorescence process", Biophysical Journal, 2003, 85(3), p1839-1850

Document 7: WO03050098A

Document 8: Chemical Abstracts, CAN: 134:115892, "Synthesis of 1,2,4-trisubstituted 2-imidazolin-5-ones", CAS RN: 52900-70-6

Document 9: Chemical Abstracts, CAN: 132:265133, "A convenient synthesis of 4-arylidene-2-phenyl-5-oxazolones catalyzed by KF-Alumina.", CAS RN: 14326-80-8

2.2 Novelty :

In Document 1, compounds such as No. 1-3 and 6-8 (see the specification p3 table 1) fall in the scope described in Claim 1. Moreover, compounds such as No. 17, 18 and 22 (see D2, the specification p8-9), compounds disclosed in table 1 (see D3, the specification p 5 ) and compounds disclosed in table 1(see D4) fall in the scope described in Claim 1. Thus, the subject matter of claim 1 is not novel and doesn't meet the criteria of novelty set out in PCT Article 33(2). Document 5 disclosed a compound represented by formula (III), which fall in the scopes described in Claims 1-3, and the preparation described in Claims 4 and 6-7. Thus, the subject matters of claims 1-4 and 6-7 are not novel and don't meet the criteria of novelty set out in PCT Article 33(2).

Furthermore, compounds such as I-3, I-11, I-15, I-17, I-19, I-20 and I-21 disclosed in Documents 6 and compounds disclosed in Documents 8-9 (CAS RN: 52900-70-6 and CAS RN: 14326-80-8) also destroy the novelty of Claims 1-2.

Since the subject matter of claims 5 and 8 are different from the disclosure of Document 1-9, claims 5 and 8 are novel.

2.3 Inventive step

Since claims 1-4 (part) and 6-7 (part) are not novel, the subject matter of claims 1-4 (part) and 6-7 (part) don't meet the criteria of inventive step set out in PCT Article 33(3).

**Supplemental Box**

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box No.V 2.Citations and explanations

D5 seems to represent the closest prior art to claim 5 and 8 (part). Considering of the teaching of D5 and general knowledge of a person skilled in the art, the person skilled in the art could easily reach the subject matters of claims 5 and 8 (part). Therefore, Claims 5 and 8 (part) are obvious and don't meet the criteria of inventive step set out in PCT Article 33(3).

D1-6 and 8-9 disclosed a part of compounds described in Claim 1, and did not provide any indication that those compounds were useful in the treatment of diseases such as Type 2 diabetes. D7 disclosed many compounds useful in the treatment of above diseases, but the structures were different from the compounds described in Claim 1. Therefore, if above compounds disclosed in D1-6 and 8-9 are disclaimed from Claim 1, the subject matter of claim1 (part) is not obvious from the disclosure in above documents. Thus, Claim1 (part) meet the criteria of inventive step set out in PCT Article 33(3). Accordingly, Claims 2-8 (part) meet the criteria of inventive step set out in PCT Article 33(3).

2.4 Industrial applicability:

Claims 1-8 meet the criteria of Industrial applicability set out in PCT Article 33(4).

**Supplemental Box**

In case the space in any of the preceding boxes is not sufficient.

Continuation of: International Patent Classification (IPC) or national classification and IPC

C07D263/42 (2006.01) i

C07D263/46 (2006.01) i

C07D277/34 (2006.01) i

C07D277/36 (2006.01) i

C07D233/70 (2006.01) i

C07D233/84 (2006.01) i

A61K31/4164 (2006.01) i

A61K31/421 (2006.01) i

A61K31/426 (2006.01) i